AF 1616

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:

Jan Endrikat et al.

Serial No.: 09/091,665 Examiner: S. Qazi

Filed: September 2, 1998 Group Art Unit: 1616

For: CONTRACEPTIVE PROCESS AND KIT FOR FEMALE MAMMALS, COMPRISING A COMBINATION OF GESTAGEN AND OESTROGEN

#18
Acharmon
1/31/02
1 of 3

BRIEF ON APPEAL UNDER 37 C.F.R. § 1.192

Honorable Commissioner for Patents
and Trademarks

Sir:

Further to the Notice of Appeal filed July 5, 2001, attached herewith are three copies of Appellants' Brief on Appeal. The attached check includes the $310.00 fee for the filing of this Brief.

This is an appeal from the decision of the Examiner finally rejecting claims 1-7 and 13-30 of the above-identified application.

(1) REAL PARTY IN INTEREST

The application is assigned of record to Schering Aktiengesellschaft, who is the real party in interest herein. The assignment is recorded in Reel 010419/Frame 0837.

(2) RELATED APPEALS AND INTERFERENCES

Appellants, their legal representative and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

09/06/2001 GTEFFERA 00000144 09091665
01 FC:120 310.00 OP

(3) STATUS OF THE CLAIMS

Claims rejected: 1-7 and 13-30

Claims allowed: (none)

Claims canceled: (none)

Claims withdrawn: 8-12 and 31-35 [but see section (4) below].

Claims on Appeal: Claims 1-7 and 13-30. A copy of the claims on appeal is provided in the attached Appendix.

(4) STATUS OF AMENDMENTS AFTER FINAL

Claims 1-7 and 13-30 are pending and are under appeal.

Claims 8-12, drawn to kits designed to be used in the methods of claims 1-7 and 13-30, were restricted from the pending claims and withdrawn from consideration by the Examiner. Appellants petitioned the restriction of these claims on July 12, 2001.

Claims 31-35, drawn to combinations designed to be used in the methods of claims 1-7 and 13-30, were restricted from the pending claims and withdrawn from consideration by the Examiner. Appellants petitioned the restriction of these claims on July 12, 2001.

(5) SUMMARY OF THE INVENTION

Appellants' invention is directed to a method of contraception in a female mammal, comprising administering a gestagen and a natural estrogen, which are combined in specific manners and administered according to particular regimens, as recited in independent claims 1, 2, 13 and 14. As can be seen from these claims, the inventive method comprises administering, over a period of at least 28 days, (a) a gestagen in an ovulation-inhibiting dose for at least 28 days, and (b) a natural estrogen for 5 to 10 days at the end of the at least 28 day period. The method of the invention allows for high contraceptive reliability as well as optimum cycle control and regular menstrual-like bleeding.

(6) ISSUES

The only issue on Appeal is whether the claims of the application are patentable under 35 U.S.C. §103.

(7) GROUPING OF THE CLAIMS

All of the claims on appeal are grouped together. Solely for the purpose of this appeal, independent claims 1, 2, 13 and 14 and those claims dependent thereon, *i.e.*, claims 3-7 and 15-30, should all fall together.

(8) APPELLANTS' ARGUMENTS

Claims 1-7 and 13-30 have been rejected under 35 U.S.C. §103 over the Neuman abstract, CA 118:161077 ("Neumann").

Claims 1-7 and 13-30 have been rejected under 35 U.S.C. §103 over USP 5,747,480 ("Gast") or USP 5,827,843 ("Koninckx"). [The rejection was originally tendered in the Office Action dated March 25, 2000 as being over Gast and Koninckx. However, because the two references were considered separately, it appears as though the rejection was actually meant to be over Gast or Koninckx, and will be treated thusly herein.]

Claims 1-7 and 13-30 have been rejected under 35 U.S.C. §103 over the Jager abstract, CA 2000438 ("Jager").

Although each of the rejections is over a different reference, the gist of the rejections is essentially the same, and is based on the allegation that each reference discloses a method of contraception involving the administration of a gestagen (*e.g.*, progestagen) and an estrogen (*e.g.*, in different references, estrogen or estradiol). In each case, as is discussed in more detail below, the manner of combining the components and/or the regimen by which they are administered differ from the instant claims. Nevertheless, the Examiner alleges that it would be obvious to modify the methods in those references to achieve the particular conditions of the instant claims, an allegation which is unfounded, and which is rebutted below.

Appellants do not dispute that Neumann, Gast, Koninckx and Jager disclose contraceptive methods which employ gestagens and estrogens. However, none of the references, taken together or separately, or knowledge available to one of skill in the art, discloses or suggests the **particular manner** in which these agents are combined, or the **schedule of their administration**, as recited in the instant claims. As is well known in the art, the levels of various hormones in female mammals vary during the menstrual cycle. Thus, for example, the levels of estrogen and progestogen, as well as other hormones, will vary cyclically in conjunction with the menstrual cycle. As a result, it is well known in the art of methods of hormonal therapy,

especially contraception, that the dosage regimen, *i.e.*, the sequence and duration of administration of particular combinations of hormonal agents, is an important factor with regard to, *e.g.*, efficacy, potential side effects, patient compliance, and the like. Moreover, many of the disclosures within the art are devoted to using different dosage regimens. Thus, the art doesn't recognize one particular dosage regime as being the optimal one. Furthermore, the very fact that two of the cited references are U.S. *patents* which claim contraceptive methods utilizing hormones (a gestagen and an estrogen) administered in different combinations and by different schedules, demonstrates the art's recognition that dosage regimen is not a mere obvious choice, but instead is used to help distinguish different methods of hormonal therapy and help establish their individual patentability.

Taking each of the cited references in turn:

Neumann

The Neuman abstract summarizes a review article which apparently discloses several forms of estrogen-progestagen drug combinations for contraception. However, the Examiner has not pointed to any disclosure in this abstract of a method comprising the particular agents and order of administration recited in the instant claims.

Gast

Gast discloses a method in which, first, a progestin/estrogen combination is administered; then, immediately following the last day of administration of the combination, estrogen *alone* is administered (see, *e.g.*, col. 10, lines 55-70 of the reference). The reference clearly does not disclose or suggest the claimed invention, *e.g.*, that estrogen and gestagen are both administered during 5-10 days at the end of the at least 28 day period.

Koninckx

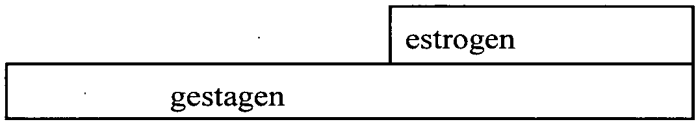
Koninckx discloses a contraceptive method in which estrogen doses oscillate such that "estrogen-dominant" and "progestogen-dominant" periods occur alternatingly, with a periodicity which is effective for optimal cycle control (see, *e.g.*, col. 1 line 67 to col. 2, lines 1-4; col. 1, lines 50-52; and examples 4 and 5). In disclosing that "the estrogen dose oscillates between two levels" (see, *e.g.*, col. 2, lines 27-29), Koninckx clearly suggests administering estrogen in pharmacologically effective amounts *throughout* the entire administration period; one of ordinary skill in the art would interpret the specification in this fashion. See also Examples 1-7 of Koninckx, which show administration of estrogen throughout the cycle. Examples 4 and 5 are

said to use estrogen doses which are "as low as possible". Koninckx fails to disclose or suggest a period of administration during which a steroidal preparation consisting essentially of a gestagen is administered (compare, *e.g.*, instant claims 1, 2 and 14), or an administration regimen in which estrogen is administered in an amount effective for achieving regular menstrual-like bleeding during only the last 5 to 10 days (compare claim 13). Furthermore, Koninckx does not disclose or suggest a gestagen-dominant period which extends for as long as 18 or more days. If anything, Koninckx discloses that, preferably, each of the gestagen-dominant or estrogen-dominant phases has a duration of less than 10 days, more preferably less than 7 days, or between 2-6 days (see, *e.g.*, Abstract and col. 2, lines 20-22). Koninckx does not even disclose that the progestogen-dominant phase is in the first part of the administration period. Compare, *e.g.*, Appellant's claim 14.

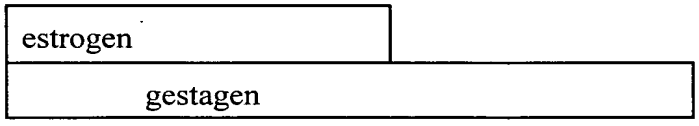
Jager

Jager does not disclose a method comprising a time period at the end of the administration cycle during which estrogen is administered. Rather, Jager administers progesterone and estrogen together during the first phase of administration, followed by a phase in which progesterone is the only active ingredient administered. See, *e.g.*, page 3, final paragraph or Example 3 (the example referred to by the Examiner). The following diagram graphically illustrates differences between Jager and a method of the instant invention.

Invention:



Jager:



In the Office Action dated April 3, 2001, the Examiner mischaracterizes Appellants' argument in the Reply of January 16, 2001 with regard to Jager. As is clear from the diagrams above, which were presented in that Reply, one difference between the instant invention and Jager is

that Jager does not disclose administering estrogen in the second phase. The Examiner's allusion to a passage in Jager which allegedly indicates that either gestagen or estrogen can be used in the first phase is irrelevant to this difference between the two methods during the second phase of administration.

The rejections with regard to the cited references fail to properly take into consideration the specific combinations and dosage schedules recited in the instant claims. It is improper to simply dismiss features recited in the claims; claimed features cannot be ignored.

> We note at the outset that the claim limitation "to form *** hydroperoxides" must be given effect since we *must* give effect to *all* claim limitations. See In re Geerdes, 491 F.2d 1260, 180 USPQ 789 (CCPA 1974); In re Wilder, 57 CCPA 1314, 419 F.2d 447, 166 USPQ 545 (1970).

In re Angstadt et al., 190 USPQ 214, 217 (CCPA 1976).

This is particularly true for factors regarding dosage regimens in methods of contraception, for the reasons discussed above.

At best, the cited references suggest that it might be "obvious to try" using the claimed combinations and schedules. However, it is well settled law that "obvious to try" does not constitute adequate motivation for an obviousness rejection. *Ex parte Argabright et al.*, 16 USPQ 703 (POBA 1967). Absent motivation, with the requisite reasonable expectation of success, to modify the methods disclosed by the references cited in the Office Actions and discussed herein so as to achieve the combinations of agents and orders of administration recited in the instant claims, the references do not render obvious the claimed invention. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

An assertion of obviousness is determined from the vantage point of a hypothetical person having ordinary skill in the art to which the patent pertains. To assess this determination, the hypothetical person has the relevant prior art references in front of him, but has **no knowledge of Appellants' invention**. Motivation is not established simply assumed by piecing together disclosures in the prior art. It is more than this. Motivation describes the rationale as to why one would be directed toward making particular modifications. The mere ability to combine parts of the prior art, by hindsight analysis, is not sufficient to establish motivation.

> ... As this court has stated, 'virtually all [inventions] are combinations of old elements ... Therefore, an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be an illogical and inappropriate process by which to determine patentability.
> *In re Rouffet*, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998)

For the reasons discussed above, the prior art fails to establish obviousness of the claimed invention. In light of the absence of a *prima facie* case of obviousness, a "showing of criticality," as demanded by the Examiner, is unwarranted and unnecessary.

It is noted that withdrawn claims 8-12, directed to kits which are designed to be used in the methods of the invention, and withdrawn claims 31-35, directed to combinations designed to be used in the methods of the invention, are patentable for at least the reasons discussed above with regard to the methods.

(9) CONCLUSION

For all of the above reasons, it is urged that the decision of the Examiner rejecting claims 1-7 and 13-30, on appeal, is in error and should be reversed.

Respectfully submitted,

Brion Heaney
Registration No. 32,542

Nancy J. Axelrod (Patent Agent)
Registration No. 44,014

Filed: September 5, 2001
K:\Sch\1637\Appeal Brief.wpd

APPENDIX OF CLAIMS ON APPEAL - SERIAL NO. 09/091,665

Claims 1-7 and 13-30:

1. A method of contraception in a female mammal, comprising administering over a period of at least 28 days

(a) a steroidal preparation consisting essentially of a gestagen in an ovulation-inhibiting dose, for at least 28 days, and

(b) a natural estrogen for 5 to 10 days at the end of said at least 28 day period.

2. A method of contraception in a female mammal, comprising administering over a period of 28 days

(a) a steroidal preparation consisting essentially of a gestagen in an ovulation-inhibiting dose, for 28 days, and

(b) a natural estrogen for 5 to 10 days at the end of said 28-day period.

3. The method according to claim 14, wherein the second phase is the last 10 days of said at least 28 day period.

4. The method according to claim 14, wherein the gestagen is
gestodene,
progesterone,
levonorgestrel,
cyproterone acetate,
chloromadinone acetate,
drospirenone (dihydrospirorenone),
norethisterone,
norethisterone acetate,
norgestimate,
desogestrel,
3-ketodesogestrel,

dienogest,

or a mixture thereof.

5. The method according to claim 14, wherein the gestagen is

levonorgestrol at 0.05-0.2 mg/day,

gestodene at 0.05-0.15 mg/day,

or another gestagen in a bioequivalent dose.

6. The method according to claim 14, wherein the gestagen is administered orally and/or transdermally.

7. The method according to claim 14, wherein the natural estrogen is administered orally and/or transdermally.

13. A method of contraception in a female mammal, comprising administering over a period of at least 28 days

(a) a gestagen in an ovulation-inhibiting dose, for at least 28 days, and

(b) a natural estrogen in an amount which is effective for achieving regular menstrual-like bleeding, during only the 5 to 10 days at the end of said at least 28 day period.

14. A method of contraception in a female mammal, comprising administering a gestagen and an estrogen over a period of at least 28 days, wherein said period has a first phase and a second phase,

wherein said first phase consists essentially of administering an ovulation-inhibiting amount of a gestagen, and said second phase comprises administering an ovulation-inhibiting amount of a gestagen and a natural estrogen in an amount effective to achieve regular menstrual-like bleeding,

wherein said second phase is the last 5 to 10 days of said period and said first phase is the remainder of said period.

15. The method of claim 14, wherein said period is 28 days.

16. The method of claim 14, wherein in the second phase, the gestagen and natural estrogen are administered in combination.

17. The method of claim 14, wherein in the second phase, the gestagen and natural estrogen are administered separately.

18. The method according to claim 14, wherein the female mammal is human.

19. The method according to claim 14, wherein the gestagen is administered orally and the natural estrogen is administered transdermally.

20. The method according to claim 14, wherein the gestagen is administered transdermally and the natural estrogen is administered orally.

21. The method according to claim 14, wherein the gestagen and the natural estrogen are administered transdermally.

22. The method according to claim 14, wherein the gestagen is levonorgestrel or gestodene.

23. The method according to claim 14, wherein the gestagen is
levonorgestrel in a dose of 0.05-0.2 mg/day, or
gestodene in a dose of 0.05-0.15 mg/day.

24. The method according to claim 14, wherein the gestagen and natural estrogen are each independently administered locally, topically, enterally, transdermally and/or parenterally.

25. The method according to claim 14, wherein
gestodene, levonorgestrel, desogestrel, 3-ketodesogestrol or a mixture thereof is administered transdermally, and
estradiol is administered transdermally at a dose of 0.025-0.25 mg of release/day.

26. The method of claim 16, wherein

during the first phase, at least 18-23 first daily dosage units of a gestagen in an ovulation-inhibiting dose are administered, and

during the second phase, at least 5 to 10 second daily dosage units of a gestagen in an ovulation-inhibiting dose plus a natural estrogen are administered.

27. The method according to claim 26, wherein 28 daily dosage units are administered; during the first phase, 18 to 23 of said first daily dosage units of a gestagen are administered; and during the second phase, 5 to 10 of said second daily dosage units of a gestagen plus a natural estrogen are administered.

28. The method according to claim 26, wherein during the second phase, 10 daily dosage units of said gestagen plus estrogen are administered.

29. The method according to claim 16, wherein the gestagen in each phase, independently, is

gestodene,
progesterone,
levonorgestrel,
cyproterone acetate,
chloromadinone acetate,
drospirenone (dihydrospirorenone),
norethisterone,
norethisterone acetate,
norgestimate,
desogestrel,
3-ketodesogestrel,
dienogest,

or a mixture thereof.

30. The method according to claim 16, wherein the gestagen in each phase is, independently,

levonorgestrel in a dose of 0.1 mg/day,

gestodene in a dose of 0.075 mg/day, or

another gestagen in a bioequivalent dosage.

K:\Sch\1637\Appeal Brief.wpd